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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,228	07/18/2007	Mark J. Ratain	ARCD:404US	4349

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EXAMINER	
HOLLERAN, ANNE L	

ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
09/16/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/591,228	RATAIN ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10-12,16-22,24-30,32,33 and 36-39* is/are pending in the application.

4a) Of the above claim(s) *36-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-12,16-22,24-30,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/9/07; 7/18/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-8, 10-12, 16-22, 24-30, 32 and 33) in the reply filed on 1/25/2010 is acknowledged.

Claims 1-8, 10-12, 16-22, 24-30, 32, 33 and 36-39 are pending.

Claims 36-39, drawn to non-elected inventions, are withdrawn from consideration.

Claims 1-8, 10-12, 16-22, 24-30, 32, and 33 are examined on the merits.

Information Disclosure Statement

Reference A10 of the IDS filed 7/9/2007 was lined through because it is a duplicate of reference A9.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 10-12, 16-22, 24-30, 32 and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 19, and 28 are indefinite because of the phrase "determining the sequence of a polymorphism in one or both EGFR genes". Does this mean determining the sequence of the entire gene and deciding if the sequence is contains a mutation? Additionally, the active step

"comprising determining the sequence" is not related to the purpose of the claimed methods of i) "evaluating the otential efficacy of an EGFR-targeting therapeutic agent", ii) "predicting the clinical prognosis for a cancer patient" or iii) "evaluating a patient's risk of toxicity to an EGFR-targeting therapeutic agent".

Claim 19 is indefinite because "the clinical prognosis" lacks antecedent basis.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10-12, 16-22, 24-30, 32 and 33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods comprising determining whether a sample from the patient contains T at position -216, and A at position -191 or both a T and an A at position -216 and -191, respectively, does not reasonably provide enablement for methods comprising determining the sequence of a polymorphism of the gene encoding EGFR, where the purpose of the methods is evaluating the potential efficacy of an EGFR-targeting therapeutic agent, predicting a clinical prognosis or evaluating a patient's risk of toxicity to an EGFR-targeting therapeutic agent, because the specification does not relate the broadly recited method of "determining a polymorphism" in one or both EGFR genes with these purposes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

The claims are broadly drawn to determining a polymorphism in one or both EGFR genes in a patient. The claims fail to relate this method step with the stated purposes of evaluating the potential efficacy of an EGFR-targeting therapeutic agent, predicting a clinical prognosis or evaluating a patient's risk of toxicity to an EGFR-targeting therapeutic agent. The claims are also broadly drawn to determining a polymorphism that is in linkage disequilibrium with polymorphisms found at specific nucleotide positions (see claims 2 and 3, for example).

The specification teaches that a T at position -216 is associated with increased expression of EGFR protein related to increased transcription of the EGFR gene (see page 37). The specification fails to teach any examples of alleles that are in linkage disequilibrium with any of the recited nucleotide position changes. The specification fails to demonstrate a correlation between any genetic polymorphisms and drug sensitivity.

Post-filing date art suggests that EGFR DNA polymorphisms are poor predictors of response to EGFR -targeted drug therapies (see Liu, W., et al., Clin. Cancer Res., 13(22): 6788-6795, 2007; page 6794, left column).

The specification does not provide an enabling disclosure of the claimed methods because the claims are broader in scope than the teachings of the specification, the specification

provides no evidence that any of the more narrowly recited methods are enabled because there is no evidence of a correlation between mutations at the specific positions identified and the stated purposes of the claimed methods, and because post-filing date art teaches that polymorphisms in the EGFR sequence are not good predictors of sensitivity to EGFR-targeted drugs. Therefore, one of skill in the art would be required to engage in further experimentation to make and use the methods as broadly claimed. This further experimentation would be undue experimentation because there is no guidance from the specification, the prior art, and the post-filing date art indictates that the finding of an increase in EGFR gene expression associated with the polymorphism at position -216 does not correlate with increased drug sensitivity.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 10-12, 19-22, 24-30, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Chi (Chi, D.D., et al. Human Molecular Genetics, 1(2): 135, 1992).

The claims are drawn to methods for evaluating the potential efficacy of an EGFR-targeting therapeutic agent for the treatment of cancer, predicting the clinical prognosis for a cancer patient, or for evaluating a patient's risk of toxicity to an EGFR-targeting therapeutic

agent. The claims as written do not relate the purpose stated in the preamble with the active step, which is that of determining the sequence of a polymorphism in one or both EGFR genes. Therefore, the claims comprise a single active step of determining at least part of the sequence of the gene encoding EGFR. The positions recited in claims 2, 3, 21, 22, 29 or 30 fail to limit the claimed inventions because the sequence of the polymorphism may be at the position or in linkage disequilibrium with a polymorphism recited in the claims. Therefore, the claims are not limited to determining polymorphisms at these positions. Additionally, it is not clear what is meant by determining the sequence of polymorphisms at these positions because a sequence is at least two nucleotides in length.

Chi teaches identifying polymorphic EGFR sequences within the first intron of the gene encoding EGFR. Chi uses PCR to sequence the first intron of the gene encoding EGFR. Because the claims encompass sequencing at least part of the gene encoding EGFR, the method of Chi is within the scope of the claims. Therefore, Chi teaches the claimed inventions.

Claims 1-8, 10-12, 16, 17,19-22, 24-30, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Gebhardt (Gebhardt, F., et al., The Journal of Biological Chemistry, 274(19): 13176-13180, 1999).

Gebhardt teaches a method comprising obtaining cancer cell lines and determining the sequence using PCR form -1439 to +2318. Because the claims encompass sequencing at least part of the gene encoding EGFR, the method of Gebhardt is within the scope of the claims. Therefore, Gebhardt teaches the claimed inventions.

Claims 1-8, 10-12, 19-22, 24-30, 32 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Shintani (Shintani, S., et al. Cancer Research, 59: 4142-4147, 1999; of record).

Shintani teaches a method comprising obtaining cancer cells lines or obtaining human oral cancer biopsis from case of oral cancer, or obtaining normal oral mucosa tissues (see page 4142, right column). Shintani teaches PCR methods to determine the sequence of part of the gene encoding EGFR (4142, right column – 4143, left column). Because the claims encompass sequencing at least part of the gene encoding EGFR, the method of Shintani is within the scope of the claims. Therefore, Shintani teaches the claimed inventions.

Claims 1-8, 10-12, 19-22, 24-30, 32 and 33 are rejected under 35 U.S.C. 102(a) as being anticipated by Liu (Liu, W., et al. Clinical Cancer Research, 9: 1009-1012, 2003, March 1).

The inventive entity of Liu is that of "another" because the inventive entity is Liu, Innocenti, Chen, Das, Cook and Ratain, whereas the inventive entity of the instant application is Ratain, Liu and Innocenti.

Liu teaches a method comprising samples from human patients (page 1009-1010). Liu teaches PCR methods to determine the sequence of part of the gene encoding EGFR (page 1010). Because the claims encompass sequencing at least part of the gene encoding EGFR, the method of Liu is within the scope of the claims. Therefore, Liui teaches the claimed inventions.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Misook Yu, can be reached on (571) 272-0839. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner

/Alana M. Harris, Ph.D./
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